

Attorney's Docket No.: 14555-003004 / 270/058

**OFFICIAL COMMUNICATION****FACSIMILE****FOR THE PERSONAL ATTENTION OF:****EXAMINER L. WELLS****GROUP 1617 FAX NO: (703) 746-5231**

Number of pages including this page 30

Applicant : Gary S. Hahn et al.  
Serial No. : 09/992,491  
Filed : November 21, 2001

Art Unit : 1617  
Examiner : L. Wells

Title : Topical Product Formulations Containing Strontium for Reducing Skin Irritation

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Attached to this facsimile communication cover sheet is a Response to Request for Information, faxed this 24<sup>th</sup> day of April, 2003, to Group 1617, the United States Patent and Trademark Office.

Respectfully submitted,



Diane L. Gardner

Reg. No. 36,518

PTO Customer No. 20985



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Attorney's Docket No.: 14555-003004 / 270/058

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Gary S. Hahn et al. Art Unit : 1617  
Serial No. : 09/992,491 Examiner : L. Wells  
Filed : November 21, 2001  
Title : TOPICAL PRODUCT FORMULATIONS CONTAINING STRONTIUM FOR  
REDUCING SKIN IRRITATION

Commissioner for Patents  
Washington, D.C. 20231

RESPONSE TO REQUEST FOR INFORMATION

In a telephone conversation on April 22, 2003, the Examiner requested additional information with respect to claims in six applications. The applications are listed as follows:

U.S. Serial No. 10/189344  
U.S. Serial No. 10/033194  
U.S. Serial No. 10/003478  
U.S. Serial No. 10/001935  
U.S. Serial No. 09/853828  
U.S. Serial No. 09/833221

The Examiner requested copies of the claims from each of the applications listed above in which the claims are drawn to strontium, as opposed to another metal.

In a follow up conversation on April 24, 2003, the Examiner confirmed that only copies of claims that are currently pending need be supplied. The single application that remains pending as of even date is U.S. Serial No. 10/189344.

## CERTIFICATE OF TRANSMISSION BY FACSIMILE

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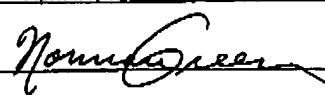
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April 24, 2003

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Applicant : Gary S. Hahn et al.  
Serial No. : 09/992,491  
Filed : November 21, 2001  
Page : 2 of 2

Attorney's Docket No.: 14555-003004 / 270/058

A Preliminary Amendment as well as a Supplemental Preliminary Amendment have been filed in this application. The pending claims are attached.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: April 24, 2003

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Attachment

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What is claimed is:

*CANCELLED*

1. A composition for topical application to an animal subject comprising a topical vehicle; an irritant ingredient contained in an amount capable of inducing skin irritation in said 5 subject; and an anti-irritant amount of aqueous-soluble divalent strontium cation.

*CANCELLED*

2. The composition of claim 1 comprising strontium cation in a concentration of from about 10 mM to about 3000 mM.

*CANCELLED*

3. The composition of claim 1 comprising strontium cation in a concentration of from 10 about 50 mM to about 2000 mM.

*CANCELLED*

4. The composition of claim 1 comprising strontium cation in a concentration of from about 100 mM to about 1000 mM.

*CANCELLED*

5. The composition of claim 1 comprising strontium cation in a concentration of from about 250 mM to about 500 mM.

*CANCELLED*

- 15 6. The composition of claim 1 comprising an amount of strontium cation capable of inhibiting mean cumulative skin irritation attributable to said irritant ingredient in a susceptible human population by at least about 20%

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**CANCELLED** 7. The composition of claim 6 wherein said inhibition of skin irritation represents an average reduction in one or more of sting, burn and itch in a susceptible human population upon topical application of said composition, as compared to the level of irritation induced in said population upon topical application of a control formulation containing said irritant ingredient in a vehicle without said strontium cation.

**CANCELLED**

8. The composition of claim 1 comprising an amount of strontium cation capable of inhibiting by at least about 40% the cumulative skin irritation attributable to said irritant ingredient in at least 10% of the susceptible human population.

**CANCELLED**

9. The composition of claim 8 wherein said inhibition of skin irritation represents an average reduction in one or more of sting, burn and itch in at least 10% of the susceptible human population upon topical application of said composition, as compared to the level of irritation induced in said at least 10% of the population upon topical application of a control formulation containing said irritant ingredient in a vehicle without said strontium cation.

**CANCELLED**

10. The composition of claim 1 wherein said composition is a cosmetic product.

**CANCELLED**

11. The composition of claim 10 wherein said composition comprises a skin exfoliant, skin peel or skin cell renewal agent.

**CANCELLED**

12. The composition of claim 10 wherein said irritant ingredient is selected from the group consisting of carboxylic acids, keto acids,  $\alpha$ -hydroxy acids,  $\beta$ -hydroxy acids, retinoids, peroxides, and organic alcohols.

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**CANCELLED** 13. The composition of claim 12 wherein said irritant ingredient comprises lactic acid or a salt thereof.

**CANCELLED** 14. The composition of claim 12 wherein said irritant ingredient comprises glycolic acid or a salt thereof.

**CANCELLED** 5 15. The composition of claim 12 wherein said irritant ingredient comprises salicylic acid or a salt thereof.

**CANCELLED** 16. The composition of claim 12 wherein said irritant ingredient comprises a combination of lactic acid and salicylic acid, or salts thereof.

**CANCELLED** 17. The composition of claim 12 wherein said irritant ingredient comprises capryloyl 10 salicylic acid or a salt thereof.

**CANCELLED** 18. The composition of claim 12 wherein said irritant ingredient comprises citric acid or a salt thereof.

**CANCELLED** 19. The composition of claim 12 wherein said irritant ingredient is a retinoid selected from tretinoin, retinol, retinal and derivatives thereof.

**CANCELLED** 15 20. The composition of claim 12 wherein said irritant ingredient comprises benzoyl peroxide.

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**CANCELLED** 21. The composition of claim 12 wherein said irritant ingredient comprises acetic acid or a salt thereof.

**CANCELLED**

22. The composition of claim 12 wherein said irritant ingredient comprises one or more of the group consisting of 1-pyrrolidone-5-carboxylic acid, capryloyl salicylic acid,  $\alpha$ -hydroxy decanoic acid,  $\alpha$ -hydroxy octanoic acid, gluconolactone, methoxypropyl gluconamide, oxalic acid, malic acid, tartaric acid, mandelic acid, benzylic acid, gluconic acid, pyruvic acid and phenol.

**CANCELLED**

23. The composition of claim 12 wherein said irritant ingredient comprises trichloroacetic acid or a salt thereof.

**CANCELLED**

24. The composition of claim 12 wherein the pH of the composition is in the range of 1 to 10 to 6.

**CANCELLED**

25. The composition of claim 12 wherein the pH of the composition is in the range of 3 to 5.

**CANCELLED**

26. The composition of claim 12 having a concentration of said irritant ingredient of from about 0.1% to about 50%

**CANCELLED**

15 27. The composition of claim 12 having a concentration of said irritant ingredient of from about 0.5% to about 20%

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**CANCELLED** 28. The composition of claim 1 wherein said composition is an antiperspirant or deodorant product.

**CANCELLED** 29. The composition of claim 1 wherein said composition is a sunscreen, tanning or sunburn treatment product.

**CANCELLED** 30. The composition of claim 1 wherein said composition is an insect repellant product.

**CANCELLED** 31. The composition of claim 10 wherein said composition is a shaving or hair removal product selected from the group consisting of depilatory, bracer, cream, foam, gel and aftershave products.

**CANCELLED** 32. The composition of claim 10 wherein said composition is a hair care or hair treatment product.

**CANCELLED** 33. The composition of claim 32 wherein said composition is selected from the group consisting of shampoo, conditioner, colorant, dye, bleach, permanent wave and hair straightener products.

**CANCELLED** 34. The composition of claim 10 wherein said composition is selected from the group consisting of cleansers, astringents, toners, rinses, serums and masks.

**CANCELLED** 35. The composition of claim 10 wherein said composition is a facial cosmetic product.

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36. The composition of claim 10 wherein said composition is selected from the group  
**CANCELLED**  
consisting of creams, lotions and moisturizers.

**CANCELLED**

37. The composition of claim 1 wherein said composition is selected from the group  
consisting of soaps and detergents.

**CANCELLED**

5 38. The composition of claim 1 wherein said composition is a topical drug product.

**CANCELLED** 39. The composition of claim 38 wherein said irritant ingredient is capsaicin.

**CANCELLED**

40. The composition of claim 38 wherein said composition is selected from the group  
consisting of antibiotic, analgesic, contraceptive, anti-acne and anti-dandruff products.

**CANCELLED**

41. The composition of claim 40 wherein said irritant ingredient is benzoyl peroxide.

10 **CANCELLED**

42. The composition of claim 1 wherein said composition is formulated as a rectal or  
vaginal suppository, foam, cream, gel or ointment.

**CANCELLED**

43. The composition of claim 1 wherein said composition is formulated for  
administration to the mouth, throat or lip.

**CANCELLED**

44. The composition of claim 43 formulated as a lozenge, mouthwash or gargle.

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**CANCELLED**  
45. The composition of claim 1 formulated as a liquid, gel, cream, emulsion, suspension or stick.

**CANCELLED**  
46. The composition of claim 1 formulated with a physical applicator.

**CANCELLED**  
47. The composition of claim 46 wherein said physical applicator is selected from the group consisting of cloths, tissues, swabs, bandages and wet wipes.

**CANCELLED**  
48. The composition of claim 1 further comprising, as counteranions to said strontium cation, one or more topically acceptable anion species.

**CANCELLED**  
49. The composition of claim 48 further comprising, as counteranions to said strontium cation, one or more anion species selected from the group consisting of nitrate, sulfate, halogen, carbonate, bicarbonate, hydroxide, oxide, peroxide, nitrite, sulfide, bisulfate, persulfate, glycerophosphate, hypophosphate, borate and titanate inorganic anions, and carboxylic acid, alkoxylate, amino acid, peptide, saturated and unsaturated organic acid, and saturated and unsaturated fatty acid organic anions.

**CANCELLED**  
50. The composition of claim 48 wherein said one or more of said counteranions is an organic anion selected from the group consisting of citrate, oxalate, acetate, gluconate, lactate, tartrate, maleate, benzoate, propionate, salicylate, ascorbate, formate, succinate, folinate, aspartate, phthalate, oleate, palmitate, stearate, lauryl sulfate, lanolate, myristate, behenate, caseinate, cyclamate, pantothenate, polyaminopolycarboxylates, saccharin, thioglycolate, laurate, methylparaben, propylparaben, ricinoleate and sorbate organic anions.

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51. The composition of claim 48 wherein said anion species includes nitrate.  
CANCELLED

CANCELLED 52. The composition of claim 48 wherein said anion species includes sulfate.

CANCELLED 53. The composition of claim 48 wherein said anion species includes a halogen selected  
from chloride and fluoride anions.

CANCELLED 54. The composition of claim 1 further comprising at least one second anti-irritant  
agent.

CANCELLED 55. The composition of claim 54 wherein the total amount of said strontium cation and  
said second agent is capable of inhibiting mean cumulative skin irritation attributable to said irritant  
ingredient in a susceptible human population by at least about 20%

*15*  
CANCELLED

10 56. The composition of claim 54 wherein the total amount of said strontium cation and  
said second agent is capable of inhibiting by at least about 40% the cumulative skin irritation  
attributable to said irritant ingredient in at least 10% of the susceptible human population.

CANCELLED 57. The composition of claim 54 wherein said second agent is selected from the group  
consisting of potassium channel mediating, regulating or blocking agents, calcium channel  
15 blocking or regulatory agents, sodium channel blocking agents, steroids, non-steroidal anti-  
inflammatory agents, aloe vera, chamomile,  $\alpha$ -bisabolol, cola nitada extract, green tea extract, tea  
tree oil, licorice extract, allantoin, urea, caffeine and other xanthenes, and glycyrrhizic acid and its  
derivatives.

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~~CANCELLED~~ 58. An composition for inhibiting skin irritation in an animal subject comprising an anti-irritant amount of aqueous-soluble divalent strontium cation and a topical vehicle.

~~CANCELLED~~ 59. The composition of claim 58 comprising strontium cation in a concentration of from  
X about 10 mM to about 3000 mM.

~~CANCELLED~~ 5 60. The composition of claim 58 comprising strontium cation in a concentration of from  
about 50 mM to about 2000 mM.

~~CANCELLED~~ 61. The composition of claim 58 comprising strontium cation in a concentration of from  
about 100 mM to about 1000 mM.

~~AMENDED~~ A.3 10 62. The composition of claim 58 comprising strontium cation in a concentration of from  
about 250 mM to about 500 mM.

~~CANCELLED~~ 63. The composition of claim 58 wherein said inhibition of skin irritation represents a  
X reduction in skin irritation attributable to a pre-existing human skin disease or skin irritation  
Y condition.

~~AMENDED~~ A.5 15 64. The composition of claim 63 wherein said skin irritation is attributable to atopic or  
allergic contact dermatitis, eczema, psoriasis or infectious disease.

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65. The composition of claim 63 wherein said skin irritation is attributable to  
**AMENDED** environmental exposure to one or more of sunlight, low humidity, wind, cold temperature, or hot  
and humid conditions.

**AMENDED** 66. The composition of claim 63 wherein said skin irritation is attributable to exposure  
5 A-7 to an irritating chemical agent.

67. The composition of claim 66 wherein said irritating chemical agent exposure is  
attributable to application of a topical product.

68. The composition of claim 67 wherein said product is selected from the group  
consisting of antiperspirant, deodorant, sunscreen, tanning, sunburn treatment, insect repellant,  
10 exfolient, skin peel, skin cell renewal, fragrance, shaving or hair removal, hair care or hair  
treatment, cleanser, astringent, toner, rinse, serum, masks, facial cosmetic, cream, lotion,  
moisturizer, soap, detergent, and topical drug products.

69. The composition of claim 67 wherein said composition is packaged with  
instructions directing administration of said composition before, with or following administration  
15 of said topical product.

70. The composition of claim 66 wherein said irritating chemical agent exposure is  
attributable to insect sting or bite, or to plant exposure.

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71. The composition of claim 63 wherein said skin irritation is attributable to one or more of shaving, skin cleansing or bathing, sweating, and physical skin trauma.

72. The composition of claim 58 wherein said skin irritation is attributable to dry skin.

73. The composition of claim 58 comprising an amount of strontium cation capable of 5 inhibiting said skin irritation in subjects experiencing the same by an average of at least about 20%

74. The composition of claim 58 comprising an amount of strontium cation capable of inhibiting said skin irritation by at least about 40% in at least 10% of the subjects experiencing the same.

75. The composition of claim 58 wherein said composition is formulated as a rectal or 10 vaginal suppository, cream, foam, gel, ointment, douche or enema.

76. The composition of claim 58 wherein said composition is formulated for administration to the mouth, throat or lip.

77. The composition of claim 76 formulated as a lozenge, mouthwash or gargle.

78. The composition of claim 58 formulated as a liquid, gel, cream, emulsion, 15 suspension or stick.

79. The composition of claim 58 formulated with a physical applicator.

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80. The composition of claim 58 further comprising, as counteranions to said strontium cation, one or more topically acceptable anion species.
81. The composition of claim 80 further comprising, as counteranions to said strontium cation, one or more anion species selected from the group consisting of nitrate, sulfate, halogen, 5 carbonate, bicarbonate, hydroxide, oxide, peroxide, nitrite, sulfide, bisulfate, persulfate, glycerophosphate, hypophosphate, borate and titanate inorganic anions, and carboxylic acid, alkoxylate, amino acid, peptide, saturated and unsaturated organic acid, and saturated and unsaturated fatty acid organic anions.
82. The composition of claim 80 wherein said one or more of said counteranions is an 10 organic anion selected from the group consisting of citrate, oxalate, acetate, gluconate, lactate, tartrate, maleate, benzoate, propionate, salicylate, ascorbate, formate, succinate, folinate, aspartate, phthalate, oleate, palmitate, stearate, lauryl sulfate, lanolate, myristate, behenate, caseinate, cyclamate, pantothenate, polyaminopolycarboxylates, saccharin, thioglycolate, laurate, methylparaben, propylparaben, ricinoleate and sorbate organic anions.
- 15 83. The composition of claim 58 further comprising at least one second anti-irritant agent.
- AMENDED A. 84. The composition of claim 83 wherein said second agent is selected from the group 20 consisting of potassium channel mediating, regulating or blocking agents, calcium channel blocking or regulatory agents, sodium channel blocking agents, steroids, non-steroidal anti-inflammatory agents, aloe vera, chamomile,  $\alpha$ -bisabolol, cola nitada extract, green tea extract, tea

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tree oil, licorice extract, allantoin, urea, caffeine and other xanthenes, and glycyrrhizic acid and its derivatives.

**AMENDED** 85. 19 A method for inhibiting skin irritation associated with an irritant ingredient contained in an applied topical formulation, comprising topically administering to an human 5 subject the composition of claim 1.

86. A method for inhibiting skin irritation in a human subject comprising topically administering to the subject the composition of claim 58.

87. The method of claim 86 wherein said composition is administered within about three hours prior to application to the subject of a second topical formulation containing an irritant 10 ingredient.

88. The method of claim 86 wherein said composition is administered substantially simultaneously with application to the subject of a second topical formulation containing an irritant ingredient.

89. The method of claim 86 wherein said composition is administered to inhibit skin 15 irritation attributable to a pre-existing human skin disease or skin irritation condition.

90. The method of claim 89 wherein said skin irritation is attributable to environmental exposure to one or more of sunlight, low humidity, wind, cold temperature, or hot and humid conditions.

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91. The method of claim 89 wherein said skin irritation is attributable to exposure to an irritating chemical agent.

92. The method of claim 89 wherein said skin irritation is attributable to one or more of shaving, skin cleansing or bathing, and physical skin trauma.

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: )  
 HAHN, Gary S. and THUESON, David O. ) Group Art Unit: To be assigned  
 Serial No.: To be assigned ) Examiner: To be assigned  
 Filed: July 3, 2002 )  
 For: FORMULATIONS AND METHODS )  
 FOR REDUCING SKIN IRRITATION )

**COPY**

## PRELIMINARY AMENDMENT

**Box Amendment**  
 Commissioner for Patents  
 Washington, D.C. 20231

Sir:

Transmitted herewith is an Amendment for the above-identified application.

IN THE SPECIFICATION:

At page 1, immediately following the title of the invention, please insert the following new paragraph:

--This application is a continuation of Serial No. 10/033,194, filed October 24, 2001, which is a continuation of Serial No. 09/853,282, filed May 10, 2001, which is a continuation of Serial No. 09/685,992, filed October 10, 2000, which is a continuation of Serial No. 08/860,993, filed June 23, 1997, and issued as U.S. Patent No. 6,139,850, which is a continuation-in-part of Serial No. 08/362,100, filed December 21, 1994 and issued as U.S. Patent No. 5,716,625. Parent

LA-241213.1

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Mauri  
 Signature of Person Mailing Paper

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application Serial No. 08/860,993 was filed nationally on June 23, 1997 pursuant to 35 U.S.C. § 371, based on International Application No. PCT/US95/16985 (filed December 21, 1995). The present application and the aforesaid PCT application claim the benefit of the filing date of Serial No. 08/362,100 (December 21, 1994), as well as the benefit of all intervening applications, pursuant to 35 U.S.C. §§ 120 and 365.--

IN THE CLAIMS:

Please amend the claims as follows:

Please cancel claims 1-61 without prejudice or disclaimer.

62. (Amended) A composition for inhibiting skin irritation in an animal subject comprising an anti-irritant amount of at least about 50 mM of aqueous-soluble divalent strontium cation and a topical vehicle, wherein said composition is packaged with instructions directing the administration of said composition to the skin of an animal subject, and wherein said composition is effective to prevent or reduce skin irritation at the skin site where the composition is administered.

Please cancel claim 63 without prejudice or disclaimer.

64. (Amended) The composition of claim 62 comprising aqueous-soluble strontium cation in a concentration of from about 50 mM to about 2000 mM.

65. (Amended) The composition of claim 62 comprising aqueous-soluble strontium cation in a concentration of from about 100 mM to about 1000 mM.

66. (Amended) The composition of claim 62 comprising aqueous-soluble strontium cation in a concentration of from about 250 mM to about 500 mM.

84. (Amended) The composition of claim 62 comprising an amount of aqueous-soluble strontium cation capable of inhibiting said skin irritation in subjects experiencing the same by an average of at least about 20%.

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85. (Amended) The composition of claim 62 comprising an amount of aqueous-soluble strontium cation capable of inhibiting said skin irritation by at least about 40% in at least 10% of the subjects experiencing the same.

95. (Amended) The composition of claim 62 further comprising, as counteranions to said aqueous-soluble strontium cation, one or more topically acceptable anion species.

96. (Amended) The composition of claim 95 further comprising, as counteranions to said aqueous-soluble strontium cation, one or more anion species selected from the group consisting of nitrate, [sulfate,] halogen, carbonate, bicarbonate, hydroxide, oxide, peroxide, nitrite, sulfide, bisulfate, persulfate, glycerophosphate, hypophosphate, borate and titanate inorganic anions, and carboxylic acid, alkoxylate, amino acid, peptide, saturated and unsaturated organic acid, and saturated and unsaturated fatty acid organic anions.

99. (Amended) The composition of claim 98 wherein said second agent is selected from the group consisting of potassium channel mediating, regulating or blocking agents, calcium channel blocking or regulatory agents, sodium channel blocking agents, steroids, non-steroidal anti-inflammatory agents, aloe vera, chamomile,  $\alpha$ -bisabolol, *Cola nitida* extract, green tea extract, tea tree oil, licorice extract, allantoin, urea, caffeine and other xanthines, and glycyrrhizic acid [and its derivatives].

Please cancel claim 100 without prejudice or disclaimer.

101. (Amended) A method for inhibiting skin irritation in an animal subject comprising topically administering to the subject a composition comprising an anti-irritant amount of at least about 50 mM of aqueous-soluble divalent strontium cation and a topical vehicle, wherein said composition is effective to prevent or reduce skin irritation at the skin site where the composition is administered [the composition of claim 62].

Please add the following new claims:

115. (New) The composition of claim 62 wherein said skin irritation is characterized by one or more of sting, burn or itch.

116. (New) The composition of claim 62 wherein said skin irritation is itch.

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117. (New) The method of claim 101 wherein said skin irritation is characterized by one or more of sting, burn or itch.

118. (New) The method of claim 101 wherein said skin irritation is itch.

119. (New) The composition of claim 62 further comprising an irritant ingredient, and wherein said composition is effective to prevent or reduce skin irritation attributable to said irritant ingredient.

120. (New) The composition of claim 119 wherein said irritant ingredient is selected from the group consisting of carboxylic acids, keto acids,  $\alpha$ -hydroxy acids,  $\beta$ -hydroxy acids, retinoids, peroxides, and organic alcohols, and the irritant ingredient is contained in said composition in an amount of at least 12% by weight.

121. (New) The composition of claim 121 wherein said irritant ingredient comprises an  $\alpha$ -hydroxy acid or a salt thereof.

122. (New) The method of claim 101 wherein said skin irritation is attributable to exposure to an irritant ingredient selected from the group consisting of carboxylic acids, keto acids,  $\alpha$ -hydroxy acids,  $\beta$ -hydroxy acids, retinoids, peroxides, and organic alcohols.

123. (New) The method of claim 122 wherein said irritant ingredient comprises an  $\alpha$ -hydroxy acid or a salt thereof.

124. (New) The method of claim 101 wherein said skin irritation is an irritation inducible by topical application of capsaicin.

125. (New) The composition of claim 68 wherein said skin irritation is attributable to eczema.

126. (New) The method of claim 104 wherein said skin irritation is attributable to eczema.

\* \* \* \* \*

The specification has been amended at page 1 to set forth related applications, to which the present application claims the benefit of priority.

The claims have been amended, and certain claims canceled, to expedite examination of the present application, and in view of subject matter already allowed in parent Application Serial No. 08/860,993 (now Patent No. 6,139,850).

Attorney's Docket No.: 14555-011005

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Gary S. Hahn et al. Art Unit : Unknown  
Serial No. : 10/189,344 Examiner : Unknown  
Filed : July 3, 2002  
Title : FORMULATIONS AND METHODS FOR REDUCING SKIN IRRITATION

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U.S. Patent and Trademark Office  
Arlington, VA 22202

## **SUPPLEMENTAL PRELIMINARY AMENDMENT**

Prior to examination, please amend the application as follows:

### In the specification:

Replace the paragraph beginning at page 17, paragraph [0035] with the following rewritten paragraph:

-- [0035] In another embodiment, the cation of the present invention may be combined in a formulation with other anti-irritants, such as steroidal or non-steroidal anti-inflammatory agents or other materials such as aloe vera, chamomile,  $\alpha$ -bisabolo, cola nitada extract, green tea extract, tea tree oil, licorice extract, allantoin, urea, caffeine or other xanthenes, glycyrrhizic acid and its derivatives, or with other anti-irritant species such as those identified in co-pending U.S. Patent Nos. 5,716,625, 5,756,625, 5,756,107, 5,804,203, 5,958,436, 6,139,850, and 6,455,076, so as to achieve a multiple-anti-irritant effect. --

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Lucille M. Begalka  
Typed or Printed Name of Person Signing Certificate

Applicant : Gary S. Hahn et al.  
Serial No. : 10/189,344  
Filed : July 3, 2002  
Page : 2

Attorney's Docket No.: 14555-002004

Replace the paragraph beginning at page 21, paragraph [0042] with the following rewritten paragraph:

[0042] The preferred concentration ranges expressed above contemplate that a typical topical dosage will be approximately 0.5 grams of cation formulation over a 5 cm x 5 cm area of skin (25 cm<sup>2</sup>). Clinical studies have shown that such preferred concentration ranges are generally effective to inhibit skin irritation and, in typical topical vehicles, are readily formulated and do not leave any significant visible residue when applied to the skin. Higher concentration formulations, such as saturated pastes or other forms, may also be successfully used, particularly where visible appearance is not a limiting consideration (as in therapeutic applications).--

Replace the paragraph beginning at page 22, paragraph [0044] with the following rewritten paragraph:

-- [0044] The optimum concentration of cation of the invention may also be reduced below (or within) the preferred ranges set forth above if some other anti-irritant component is included in the formulation along with the cation component of the invention. In particular, it is contemplated that lower (e.g. halved) amounts of strontium (SR<sup>2+</sup>) cations may be used, while still maintaining comparable levels of anti-irritant activity, by further including an approximately equal concentration of, for example, a potassium channel mediating, regulating or blocking agent, a calcium channel blocking or regulatory agent, or a sodium channel blocking agent, or other anti-irritant agent such as a steroid or non-steroidal anti-inflammatory agent. Examples of suitable additional anti-irritant ingredients are described in applicants' co-pending U.S. Patent Nos. 5,716,625, 5,756,625, 5,756,107, 5,804,203, 5,958,436, 6,139,850, and 6,455,076, and incorporated by reference in their entirety. --

In the claims:

Amend claims 72-76, 76-80, 83, 86 as follows:

~~72.~~ (Amended) The composition of claim 62 wherein said skin irritation is attributable to dry skin.

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73. (Amended) The composition of claim 62 comprising an amount of strontium cation capable of inhibiting said skin irritation in subjects experiencing the same by an average of at least about 20%.

74. (Amended) The composition of claim 62 comprising an amount of strontium cation capable of inhibiting said skin irritation by at least about 40% in at least 10% of the subjects experiencing the same.

75. (Amended) The composition of claim 62 wherein said composition is formulated as a rectal or vaginal suppository, cream, foam, gel, ointment, douche or enema.

76. (Amended) The composition of claim 62 wherein said composition is formulated for administration to the mouth, throat or lip.

78. (Amended) The composition of claim 62 formulated as a liquid, gel, cream, emulsion, suspension or stick.

79. (Amended) The composition of claim 62 formulated with a physical applicator.

80. (Amended) The composition of claim 62 further comprising, as counteranions to said strontium cation, one or more topically acceptable anion species.

83. (Amended) The composition of claim 62 further comprising at least one second anti-irritant agent.

86. (Amended) A method for inhibiting skin irritation in a human subject comprising topically administering to the subject the composition of claim 62.

121. (Amended) The composition of claim 101 wherein said irritant ingredient comprises an  $\alpha$ -hydroxy acid or a salt thereof.--

Please add the following new claims:

127. (New) The composition of claim 62 formulated as a liquid gel, cream, emulsion, suspension or stick.

128. (New) The composition of claim 62 formulated with a physical applicator.

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129. (New) The composition of claim 95 wherein said one or more of said counteranions is an organic anion selected from the group consisting of citrate, oxalate, acetate, gluconate, lactate, tartrate, maleate, benzoate, propionate, salicylate, ascorbate, formate, succinate, folinate, aspartate, phthalate, oleate, palmitate, stearate, lauryl sulfate, lanolate, myristate, behenate, caseinate, cyclamate, pantothenate, polyaminopolycarboxylates, saccharin, thioglycolate, laurate, methylparaben, propylparaben, ricinoleate and sorbate organic anions.

130. (New) The composition of claim 62 further comprising at least one second anti-irritant agent.

131. (New) The method of claim 101 wherein said composition is administered within about three hours prior to application to the subject of a second topical formulation containing an irritant ingredient.

132. (New) The method of claim 101 wherein said composition is administered substantially simultaneously with application to the subject of a second topical formulation containing an irritant ingredient.

133. (New) The method of claim 101 wherein said composition is administered to inhibit skin irritation attributable to a pre-existing animal skin disease or skin irritation condition.

134. (New) The method of claim 101 wherein said skin irritation is ocular irritation.

135. (New) The method of claim 101 wherein said skin irritation is respiratory system irritation.

136. (New) The method of claim 101 wherein said skin irritation is gastrointestinal system irritation.

137. (New) The method of claim 101 wherein said skin irritation is reproductive system irritation.

138. (New) The method of claim 101 wherein said skin irritation is irritation of a mucous membrane.

139. (New) The method of claim 101 wherein said skin irritation is irritation of epidermal skin.

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140. (New) The method of claim 101 wherein said skin irritation is irritation of dermal skin.

141. (New) The method of claim 133 wherein said skin irritation is attributable to environmental exposure to one or more of sunlight, low humidity, wind, cold temperature, or hot and humid conditions.

142. (New) The method of claim 133 wherein said skin irritation is attributable to exposure to an irritating chemical agent.

143. (New) The method of claim 133 wherein said skin irritation is attributable to one or more of shaving, skin cleansing or bathing, and physical skin trauma.--

In the abstract:

Insert the abstract as follows.

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ABSTRACT

Compositions and methods are provided for inhibiting skin irritations attributable to chemical irritants or environmental conditions by the application of anti-irritant amounts of aqueous-soluble divalent strontium cation.--

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REMARKS

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be examined. No fee is believed to be due, however, please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: September 30, 2002

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Version with markings to show changes made

In the specification:

Paragraph beginning at page 17, paragraph [0035] has been amended as follows:

[0035] In another embodiment, the cation of the present invention may be combined in a formulation with other anti-irritants, such as steroid or non-steroidal anti-inflammatory agents or other materials such as aloe vera, chamomile,  $\alpha$ -bisabolo, cola nitada extract, green tea extract, tea tree oil, licorice extract, allantoin, urea, caffeine or other xanthenes, glycyrrhizic acid and its derivatives, or with other anti-irritant species such as those identified in co-pending U.S. Patent [Application Serial] Nos. [ / ], [ / ], [ / ] and [ / ], (attorney docket numbers 210/181, 210/182, 210/183, and 210/184, entitled "Formulations and Methods for Reducing Skin Irritation"), filed on December 21, 1994 by the present inventors] 5,716,625, 5,756,625, 5,756,107, 5,804,203, 5,958,436, 6,139,850, and 6,455,076, so as to achieve a multiple-anti-irritant effect.

Paragraph beginning at page 21, paragraph [0042] has been amended as follows:

[0042] The preferred concentration ranges expressed above contemplate that a typical topical dosage will be approximately 0.5 grams of cation formulation over a 5 cm x 5 cm area of skin (25 cm<sup>2</sup>). Clinical studies have shown that such preferred concentration ranges are generally effective to inhibit skin irritation and, in typical topical vehicles, are readily formulated and do not leave any significant visible residue when applied to the skin. Higher concentration formulations, such as saturated pastes or other forms, may also be successfully used, particularly where visible [apeparance] appearance is not a limiting consideration (as in therapeutic applications).

Paragraph beginning at page 22, paragraph [0044] has been amended as follows:

[0044] The optimum concentration of cation of the invention may also be reduced below (or within) the preferred ranges set forth above if some other anti-irritant component is included in the formulation along with the cation component of the invention. In particular, it is

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contemplated that lower (e.g. halved) amounts of strontium ( $SR^{2+}$ ) cations may be used, while still maintaining comparable levels of anti-irritant activity, by further including an approximately equal concentration of, for example, a potassium channel mediating, regulating or blocking agent, a calcium channel blocking or regulatory agent, or a sodium channel blocking agent, or other anti-irritant agent such as a steroid or non-steroidal anti-inflammatory agent. Examples of suitable additional anti-irritant ingredients are described in applicants' co-pending U.S. Patent [Application Serial] Nos. [ / ], [ / ], [ / ] and [ / ] (attorney docket numbers 210/181, 210/182, 210/183, and 210/184, entitled "Formulations and Methods for Reducing Skin Irritation"), filed December 21, 1994] 5,716,625, 5,756,625, 5,756,107, 5,804,203, 5,958,436, 6,139,850, and 6,455,076, and incorporated by reference in their entirety.

In the claims:

Claims 54-62 have been added.

Claims 72-76, 78-80, 83, 86 and 121 have been amended as follows:

72. (Amended) The composition of claim [58] 62 wherein said skin irritation is attributable to dry skin.

73. (Amended) The composition of claim [58] 62 comprising an amount of strontium cation capable of inhibiting said skin irritation in subjects experiencing the same by an average of at least about 20%.

74. (Amended) The composition of claim [58] 62 comprising an amount of strontium cation capable of inhibiting said skin irritation by at least about 40% in at least 10% of the subjects experiencing the same.

75. (Amended) The composition of claim [58] 62 wherein said composition is formulated as a rectal or vaginal suppository, cream, foam, gel, ointment, douche or enema.

76. (Amended) The composition of claim [58] 62 wherein said composition is formulated for administration to the mouth, throat or lip.

78. (Amended) The composition of claim [58] 62 formulated as a liquid, gel, cream, emulsion, suspension or stick.

79. (Amended) The composition of claim [58] 62 formulated with a physical applicator.

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80. (Amended) The composition of claim [58] 62 further comprising, as counteranions to said strontium cation, one or more topically acceptable anion species.

83. (Amended) The composition of claim [58] 62 further comprising at least one second anti-irritant agent.

86. (Amended) A method for inhibiting skin irritation in a human subject comprising topically administering to the subject the composition of claim [58] 62.

121. (Amended) The composition of claim [121] 101 wherein said irritant ingredient comprises an  $\alpha$ -hydroxy acid or a salt thereof.